II. REMARKS

Preliminary Remarks

Amendment of the Specification

The specification is amended to describe the deposited material, identify the name and address of the depository, and the date and designation numbers of the deposits, pursuant to 37 C.F.R. § 1.809(d).

Amendment of the Claims

Claims 15 and 36 are amended.

Claim 15 is amended to be directed to a murine monoclonal antibody or immunologically reactive fragment thereof which recognizes and binds to a protein complex comprising a two-chain form of matriptase, which antibody is selected from the group consisting of M69 and M123. Support for this amendment is found in the specification, *e.g.*, in Example 5 (pages 89-91), which describes antibodies M69 and M123 as antibodies that selectively bind with greater affinity to a two-chain (active) form of matriptase of a human than to a single-chain (zymogen) form of matriptase of said human.

Claim 36 is amended to specify that the antibody or immunologically reactive fragment thereof of claim 16 binds to the two-chain (active) form of a matriptase protein that is present in a complex comprising (HAI-1) or a fragment thereof, as described, *e.g.*, on pages 3 and 90-91.

Patentability Remarks

Scope of enablement

Claims 15 and 19 were newly rejected under 35 U.S.C. §112, First Paragraph, as allegedly failing to comply with the requirement for enablement, to the extent that antibodies M32, M69, and M19 are necessary to practice the claimed invention but are not known and readily available to the public or obtainable by a reproducible method described in the specification.

Claim 15 is amended to be directed to a murine monoclonal antibody selected from the group consisting of M69 and M123. As stated in the new paragraph added by amendment

to the specification, hybridomas M69 and M123, which produce antibodies M69 and M123, respectively, were deposited on September 28, 2005, with the American Type Culture Collection (ATCC), currently located at 10801 University Boulevard, Manassas, VA 20110-2209, under the provisions of the Budapest Treaty. Submitted herewith is a Declaration of Biological Deposit in Compliance with the Budapest Treaty, executed by the undersigned attorney of record, which states that the above-described deposits have been made under the terms of the Budapest Treaty, and that all restrictions on the availability to the public of the cell lines so deposited will be irrevocably removed upon the granting of the patent. Accordingly, withdrawal of the rejection of claims 15 and 19 under 35 U.S.C. §112, First Paragraph, for lack of enablement is respectfully requested.

Written Description

(A) Claims 16, 18, and 34-36 were newly rejected under 35 U.S.C. §112, First Paragraph, because the claims allegedly contain subject matter that is "not described by the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

Claim 16 is directed to:

"[a]n isolated antibody or immunologically reactive fragment thereof which selectively binds with greater affinity to a two-chain (active) form of matriptase of a human than to a single-chain (zymogen) form of matriptase of said human."

In the statement of the rejection, the examiner acknowledged that the application describes isolating antibodies M69 and M123 and demonstrates that both antibodies have the identifying characteristic of being able to selectively bind with greater affinity to a two-chain, active form of a human matriptase than to a single-chain, zymogen form of matriptase, as specified in claim 16. Moreover, the examiner cited an excerpt from the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, Friday, January 5, 2001, pages 1099-1111, see page 1106) which states that "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a), above), reduction to drawings (see (1)(b), above), or by disclosure of relevant, identifying characteristics, *i.e.*, ... functional characteristics coupled with a known or disclosed correlation between function and structure ... sufficient to

show the applicant was in possession of the claimed genus .... (citing Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998), emphasis added). However, the examiner alleged that the requirement for written description is not satisfied because the applicants "have not provided any means of determining what epitope[s] these antibodies target so as to allow those in the art to identify and (sic) particular structure that may be targeted which structure would correspond to an epitope present in the two-chain but not in the zymogen form of matriptase."

The examiner states that the rejected claims also lack written description because the specification does not provide deposit or sequence information that would enable one to reproducibly obtain claimed antibodies M69 or M123 in order to be able to identify the specific epitopes in matriptase to which they bind. The examiner adds that even if the application did describe the specific epitopes in matriptase that are bound by antibodies M69 and M123, written description would still be lacking, because the application "would provide little description relevant to determining what other epitopes may be targeted to achieve the same function." (see page 7 of the official action).

The applicants submit that the specification **does** provide written description of the subject matter of claims 16, 18, and 34-36 in compliance with the written description requirement of 35 U.S.C. §112, First Paragraph, as discussed under the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, Friday, January 5, 2001, pages 1099-1111; and in section 2163 of the M.P.E.P.

The antibodies that are the subject of claims 16, 18, and 34-36 are clearly described in the application as having the identifying functional characteristic of being able to selectively bind with greater affinity to a two-chain (active) form of matriptase of a human than to a single-chain (zymogen) form of matriptase of said human. The application describes methods that use a combination of known and reliable screening and assay procedures by which the claimed antibodies can be obtained. In particular, Example 5 describes screening 80 hybridoma clones that bind specifically to the 95 kDa matriptase/KPSI complex under non-boiled conditions and to uncomplexed matriptase after boiling, and identifying hybridomas M69 and M123 that produce antibodies that selectively bind with greater affinity

to a two-chain (active) form of a human matriptase than to a single-chain (zymogen) form of human matriptase (*e.g.*, see page 90, line 7, to page 91, line 10). The electrophoretic assay used in the disclosed example to identify antibodies according to claim 16 is a generic assay that detects binding to any portion of either the single-chain form or the two-chain form of matriptase. Given that screening 80 hybridomas that bind specifically to the 95 kDa matriptase/KPSI complex resulted in identification of two hybridomas that produce antibodies within the genus of the claims, as described in the application, a person of skill in the relevant art would reasonably expect that by screening a larger number of hybridomas that bind specifically to the 95 kDa matriptase/KPSI, one could obtain other hybridomas that produce antibodies that also selectively bind with greater affinity to a two-chain (active) form of a human matriptase than to a single-chain (zymogen) form of human matriptase, as specified in claim 16.

The examiner's statement that claims 16, 18, and 34-36 lack written description because the application does not provide a means for determining an epitope that is bound by the claimed antibodies is not relevant to the invention that is described by the application. A U.S. patent application with claims directed to antibodies that bind specifically to a target molecule does not have to describe a method for determining a specific epitope that is bound by the claimed antibodies in order to satisfy the written description requirement of 35 U.S.C. §112, First Paragraph.

> "An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, page 1106 (citations omitted, emphasis added).

> "For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). See footnote no. 42 of the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, page 1110 (emphasis added).

As shown by the above excerpts from the Guidelines for the written description requirement, binding affinity and/or binding specificity are identifying characteristics of a claimed antibody, the description of which can be sufficient to show possession of the claimed antibody to one of skill in the art at the time of filing. The application does not have to describe a method for determining an epitope bound by the claimed antibodies in order to comply with the written description requirement of 35 U.S.C. §112, First Paragraph.

The examiner rejected claims 16, 18, and 34-36 for an alleged lack written description because the specification does not provide deposit information with respect to hybridomas M69 and M123. The applicants submit that hybridoma M69 and hybridoma M123, which produce antibodies M69 and M123, respectively, were deposited with the ATCC under the provisions of the Budapest Treaty, as discussed above and in the accompanying Declaration of Biological Deposit in Compliance with the Budapest Treaty. A copy of the receipt from the ATCC for the deposit of hybridomas M69 and M123 is also enclosed.

Withdrawal of the rejection of claims 16, 18, and 34-36 under 35 U.S.C. §112, First Paragraph, for failure to comply with the written description requirement, is respectfully requested in view of the foregoing.

(B) Claim 36 was further rejected under 35 U.S.C. §112, First Paragraph, as failing to comply with the written description requirement, because the only Kunitz-type serine protease inhibitor described by the application as forming a complex with the disclosed human matriptase protein is HAI-1. As noted above, claim 36 is amended to specify that the antibody or immunologically reactive fragment thereof of claim 16 binds to the two-chain (active) form of a matriptase protein that is present in a complex comprising (HAI-1) or a fragment thereof. Withdrawal of the rejection of claim 36 under 35 U.S.C. §112, First Paragraph, for lack of written description with respect to the nature of the inhibitor in the complex is therefore respectfully requested.

III. IN CONCLUSION

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If the examiner identifies any points that he feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

No fees are believed to be due, however, please charge any fees associated with the submission of this response to Deposit Account Number 033975.

Respectfully submitted,
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